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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,110	02/24/2005	Qishou Xu	CU-4057 BWH	3549

26530 7590 05/14/2008

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EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
4131	
MAIL DATE	DELIVERY MODE
05/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,110	XU ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *4 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 9-20* is/are rejected.

7)☒ Claim(s) *3 and 6-8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *16 May 2005 and 11 August 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a National Stage entry of PCT/CN03/00609 filed on 29 July 2003 and claims priority to China foreign application 02125917.8 filed on 2 August 2002. A certified copy of the foreign priority document in Chinese has been received. No English translation has been provided.

Information Disclosure Statement

The information disclosure statement (IDS) dated 16 May 2005 and 11 August 2006 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, they have been placed in the application file and the information therein has been considered as to the merits.

Election/Restrictions

Since applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election without traverse of Group I, claims 1-3 and 6-20, drawn to a compound of formula (I) and composition comprising the same, in the reply filed on 4 February 2008 is acknowledged.

Claims 4-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4 February 2008.

Claim Objections

Claims 6-7 are objected to because of the following informalities: The abbreviation in the recitation of "A w/o suspending preparation..." should be spelled out as "water in oil".

Claims 10 and 15-16 are objected to because of the following informalities: The recitation of "bone marrow transportation" in these claims should be replaced with "bone marrow transplantation". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 9-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of a "derivative" in claim 1 renders the claim herein indefinite. The recitation of "ester derivatives of riboflavin" is not clearly defined in the specification. The 10th edition of the Merriam-Webster's Collegiate Dictionary (Merriam-Webster Incorporated: Springfield, Massachusetts, 1993, pp 311) defines "derivative" as, "a chemical substance related structurally to another substance and theoretically derivable from it." Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to "ester derivative of riboflavin"

herein. Thus, it is unclear and indefinite as to how the "derivative" herein is encompassed thereby.

The recitation of what the applicants are claiming in claims 9-20 renders the claims herein indefinite because the claims can be interpreted in two ways. First, the recitation "…in preparing the medicament for…" suggests that the claim is directed to an intended use of the composition. Second, the recitation of "An application of the compound…" suggests that the claim is directed towards a method of treatment comprising administration of the compound. Therefore, it is unclear what the applicants intend to claim.

It is suggested that the applicants amend the claims in accordance with what they intend to claim. In order to expedite prosecution, claims 9-20 will be interpreted as a method of treatment, and examined herein as such.

Claims 9-20 provide for the use of the compound, as interpreted by Examiner from the recitation of "An application of the compound…", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9-20 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, as interpreted by Examiner from the recitation of "An application of the compound…", without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-11, 13, 15 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of a medicament comprising the compound of formula (II) for treatment of ariboflavinosis, digestive tract catarrh, and persistent oral ulcer, does not reasonably provide enablement for the preparation of a medicament comprising other ester derivatives of riboflavin for treatment of ariboflavinosis, digestive tract catarrh, persistent oral ulcer, coronary heart disease, hypertension syndrome, arthritis and burn wound.

Claims 12 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of a medicament comprising the compound of formula (II) for treatment of ariboflavinosis, digestive tract catarrh, and

persistent oral ulcer, does not reasonably provide enablement for the treatment of coronary heart disease, hypertension syndrome, arthritis and burn wound.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn an application of the compound in claims 1 or 2, wherein the compound can be used in preparing the medicament for ariboflavinosis, digestive tract catarrh, persistent oral ulcer, coronary heart disease, hypertension syndrome, arthritis and burn wound.

Breadth of claims: The claims are extremely broad in that they encompass literally all the various ester derivatives of riboflavin.

Amount of guidance/Existence of working examples: Working examples are present which only show that the compound of formula (II) are effective when prepared as a medicament for ariboflavinosis, digestive tract catarrh, persistent oral ulcer, coronary heart disease, hypertension syndrome, arthritis and burn wound. There is no guidance in the specification, nor are there any working examples, to show that any other claimed ester derivatives of riboflavin are effective as a medicament for ariboflavinosis, digestive tract catarrh, persistent oral ulcer, coronary heart disease, hypertension syndrome, arthritis and burn wound.

State of the prior art/Predictability or unpredictability of the art: The prior art teaches that riboflavin is used therapeutically to ameliorate ariboflavinosis (PTO-892, ref. A), and that riboflavin in combination with amino acids and effectors of the urea cycle are effective in alleviating or reducing the effects of fatigue and weakness associated with cancer and cytotoxic cancer chemotherapy (PTO-892, ref. B). Furthermore, the prior art teaches that riboflavin-5'-monobutyrate and riboflavin tetrabutyrate have the same nutritional activity as riboflavin, suggesting that the ester compounds are easily hydrolyzed to riboflavin. On the other hand, the prior art also teaches that riboflavin-5'-monopalmitate has very little riboflavin activity while riboflavin tetrapalmitate does not have any riboflavin activity because these ester compounds are slow to hydrolyze to riboflavin (PTO-892, ref. V). This suggests that only small ester modifications of riboflavin are efficiently converted to the natural riboflavin compound and larger ester modifications of riboflavin are not converted to riboflavin very efficiently.

Therefore, in view of the *Wands* factors as discussed above, there is no clear and convincing evidence in sufficient support of the use of all the claimed ester derivatives of riboflavin in preparing the medicament for ariboflavinosis, digestive tract catarrh, and persistent oral ulcer, nor is there any clear and convincing evidence in sufficient support of the use of the compound of formula (II) in the treatment of coronary heart disease, hypertension syndrome, arthritis and burn wound.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by research publication by Edwards *et al*. (J. Photochem. Photobiol. B: Biol. 1999).

Edwards *et al.* discloses the photochemical and pharmacokinetic properties of selected flavin compounds. The compounds include riboflavin, lumiflavin and the 2', 3', 4', 5'-tetraacetyl, -tetrapropionyl, -tetrabutyrl and -tetrapalmitoyl esters of riboflavin (abstract). These compounds are shown in figure 1 (p. 37).

The tetrapropionyl ester of riboflavin, shown in figure 1 wherein R_2 is -$COCH_2CH_3$, disclosed by Edwards *et al.*, anticipates claims 1-2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Section [0001]

Claims 9, 11, 13 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over research publication by Edwards *et al.* (J. Photochem. Photobiol. B: Biol. 1999) as applied to claims 1-2 above, and further in view of Okuda *et al.* (Chem. Pharm. Bull. 1980) and US Patent No. 6,565,891 to Chandra (herein referred to as the '891 patent).

The teachings of Edwards *et al.* were as described above in the claim rejections under 35 USC § 102. Edwards *et al.* does not teach the preparation of a medicament for ariboflavinosis or persistent oral ulcer, wherein the medicament contains a compound of formula (1).

Okuda *et al.* teaches nutritional and ariboflavinosis-curing effects of riboflavin-5'-monobutyrate and monopalmitate. To test the nutritional effects of the riboflavin derivatives, rats were fed either a standard diet, a riboflavin-deficient diet, a riboflavin-deficient diet supplemented with riboflavin-5'-monobutyrate suspended in olive oil, or a riboflavin-deficient diet supplemented with riboflavin-5'-monopalmitate suspended in olive oil (p. 9, under subheading "methods"). The authors previously showed that riboflavin tetrabutyrate had the same vitamin B_2 activity (nutritional and ariboflavinosis-curing effects) in young rats as riboflavin, but riboflavin tetrapalmitate did not have vitamin B_2 activity as rats administered riboflavin tetrapalmitate clearly showed ariboflavinosis. Similar to riboflavin tetrabutyrate, rats fed a diet supplemented with riboflavin-5'-monobutyrate exhibited vitamin B_2 activity (p. 13, second full paragraph). However, rats fed a diet supplemented with riboflavin-5'-monopalmitate showed signs of lower vitamin B_2 activity. Their results suggest that riboflavin-5'-monobutyrate is easily

hydrolyzed to riboflavin, and hence has the same nutritional effect as riboflavin, while riboflavin-5'-monopalmitate was only slowly hydrolyzed to riboflavin (p. 13, last paragraph).

The '891 patent teaches a nutritional supplement for children that is most effective in optimizing health, increasing the immunity, and decreasing the instances and severity of infection, particularly among children (abstract). The importance of each of the component vitamins and minerals making up the nutritional supplement is described in detail. Of particular relevance, is the importance of riboflavin in the nutritional supplement. The '891 patent teaches that riboflavin participates in oxidation-reduction reactions in numerous metabolic pathways and in energy production via the respiratory chain (column 7, lines 22-31). It is used therapeutically to ameliorate ariboflavinosis resulting from diverse causes such as inadequate dietary intake, decreased assimilation, rare genetic defects in the formation of specific flavoproteins, hormonal disorders and after use of certain drugs. Symptoms indicating riboflavin deficiency include rough skin, angular stomatitis, cracked lips, and mouth ulcers.

It is noted that the Okuda *et al.* reference teaches the administration of compounds specifically excluded in the instant claims. However, the compounds have close structural similarity to non-excluded compounds as described by Edwards *et al.*, i.e. tetrapropionyl ester of riboflavin compared to excluded compound tetrabutyryl ester of riboflavin. Moreover, as suggested by Edwards *et al.*, short chain esters of riboflavin exhibit similar biochemical properties to other short chain esters of riboflavin (such as acetyl and propionyl esters) and likewise, longer-chain esters exhibit biochemical

characteristics similar to other longer-chain esters (such as butyryl esters and palmitoyl esters) (abstract). Also, see below for recitation of section from MPEP § 2144.09 regarding structural homologs.

The following is a quotation of MPEP § 2144.09:

> **Compounds which are** position isomers (compounds having the same radicals in physically different positions on the same nucleus) or **homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity** that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Edwards *et al.*, concerning the photochemical and pharmacokinetic properties of selected riboflavin compounds, with the teachings of Okuda *et al.*, regarding nutritional and ariboflavinosis-curing effects of riboflavin-5'-monobutyrate and monopalmitate, with the teachings of the '891 patent, regarding a nutritional supplement for children. Given the state of the art at the time of the invention, it would have been *prima facie* obvious for one of ordinary skill to test the efficacy of these homologous compounds in treating ariboflavinosis.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0002]

Claims 10 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over research publication by Edwards *et al.* (J. Photochem. Photobiol. B: Biol. 1999) as applied to claims 1-2 above, and further in view of Okuda *et al.* (Chem. Pharm. Bull. 1980), and PG Publication No. US 2003/0105104 A1 by Burzynski.

The teachings of Edwards *et al.* were as described above in the claim rejections under 35 USC § 102 and the teachings of Okuda *et al.* were as described above in section [0001] of the claim rejections under 35 USC § 103. Edwards *et al.* and Okuda *et al.* do not teach the preparation of a medicament for digestive tract catarrh caused by bone marrow transportation, leukemia or chemotherapy, wherein the medicament contains a compound of formula (1).

Burzynski teaches a pharmaceutical composition comprising riboflavin, effectors of the urea cycle, and amino acids, suitably combined with appropriate carriers, diluents, or excipients (abstract; paragraph 0001 and 0008; claim 14), as well as a method for alleviating or reducing the toxic, nutritional and metabolic disturbances associated with cancer and cancer chemotherapy by administering the said composition to a cancer patient in need thereof (paragraph 0024; claim 1). Common side effects associated with cancer treatment include tiredness, loss of appetite, mucositis, diarrhea and myelosuppression (paragraph 0072). In example 1 (paragraphs 0070-0073), Burzynski shows that when a female patient diagnosed with adenocarcinoma of the colon was administered a composition comprising a sterile solution of six amino acids, L-arginine, and riboflavin prior to treatment by chemotherapy with 5-fluorouracil, the patient did not experience the side effects typically associated with the chemotherapy treatment.

McCarthy *et al.* teaches risk factors associated with mucositis in patients receiving 5-fluorouracil chemotherapy for cancer of the digestive tract. Oral mucositis is a dose-limiting toxicity of 5-fluorouracil and includes inflammation and ulceration of the

oral mucosa and myelosuppression (abstract; p. 484, column 2). Although no direct relationship could be drawn, their results suggest that a lower neutrophil count is associated with the development of oral mucositis during therapy (p. 488, column 2, last paragraph).

It is noted that the Burzynski reference does not specifically teach the administration of ester analogs of riboflavin to cancer patients exhibiting the common side effects of chemotherapy. However, as described above in section [0001] of the claim rejections under 35 USC § 103, Okuda *et al.* teaches that esters of riboflavin can be hydrolyzed to the natural riboflavin compound and thus exhibit activity similar to riboflavin. Therefore, esters of riboflavin can serve as functional substitutes for natural riboflavin when administered in a composition.

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Edwards *et al.*, concerning the photochemical and pharmacokinetic properties of selected riboflavin compounds, with the teachings of Okuda *et al.*, regarding nutritional and ariboflavinosis-curing effects of riboflavin-5'-monobutyrate and monopalmitate, with the teachings of Burzynski, regarding a pharmaceutical composition comprising riboflavin, effectors of the urea cycle and amino acids, with the teachings of McCarthy *et al.*, regarding the risk factors associated with mucositis in patients receiving 5-fluorouracil chemotherapy for cancer of the digestive tract. One would have been motivated to combine the teachings in order to receive the expected benefit, as suggested by Edwards *et al.*, that the increase in

hydrophobicity of the ester compounds of riboflavin enhance its affinity for tumors and other kinds of proliferating cells (p. 37, column 1).

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0003]

Claims 12 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over research publication by Edwards *et al*. (J. Photochem. Photobiol. B: Biol. 1999) as applied to claims 1-2 above, and further in view of Nagatomo *et al.* (Acta Med. Biol. 1982).

The teachings of Edwards *et al.* were as described above in the claim rejections under 35 USC § 102. Edwards *et al.* does not teach the preparation of a medicament for coronary heart disease, hypertension syndrome, arthritis and burn wound, wherein the medicament contains a compound of formula (1).

Nagatomo *et al.* teaches the effects of riboflavin tetrabutyrate (RBF) on cardiohemodynamics and myocardial energy metabolism in epi- and endocardium during ischemic periods. RBF is hydrolyzed by pancreatic lipase to produce natural riboflavin and butyric acid in the body. In cardiac muscle, it is present as flavin-adenine dinucleotide (FAD) and plays a crucial role in transporting the hydrogen ion from substrate to enzymes or cytochromes (p. 136). It is well known that significant depletion of high energy phosphates occurs in the ischemic canine heart after ligation of the coronary artery, leading to the deterioration of cellular function and cell membrane

integrity. Energy production in the myocardium under normal conditions depends largely on oxidative phosphorylation. ATP produced via this route serves as the immediate source of energy for excitation-contraction coupling of the myocardium (p. 144). As shown in figure 3 (p. 140), administration of RBF to ischemic canine induces an increase of ATP concentration in the ischemic heart (p. 142). Nagatoma *et al.* concludes that RBF protects the canine heart from ischemic derangements through improvement of the energy metabolism and/or beneficial hemodynamic effects.

It is noted that the Nagatomo *et al.* reference teaches the administration of a compound specifically excluded in the instant claims. However, riboflavin tetrabutyrate has close structural similarity to a non-excluded compound described by Edwards *et al.*, i.e. tetrapropionyl ester of riboflavin. Therefore, one of ordinary skill in the art would expect the compounds to exhibit similar properties. See below for recitation of section from MPEP § 2144.09 regarding structural homologs.

The following is a quotation of MPEP § 2144.09:

> **Compounds which are** position isomers (compounds having the same radicals in physically different positions on the same nucleus) or **homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity** that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Edwards *et al.*, concerning the photochemical and pharmacokinetic properties of selected riboflavin compounds, with the teachings of Nagatomo *et al.*, regarding the effects of riboflavin tetrabutyrate (RBF) on cardiohemodynamics and myocardial energy metabolism in epi- and endocardium during ischemic periods. One would have been motivated to combine the teachings in

order to receive the expected benefit, as suggested by Edwards *et al.*, that ester analogs of riboflavin can function as phototherapeutic agents for the treatment of selected diseases (p. 37, column 1).

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Allowable Subject Matter

Claims 3 and 6-8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The compound of formula (II) is found to be free of the prior art.

Conclusion

Claims 1-2 and 9-20 are rejected.

Claims 3 and 6-8 are objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Cecilia Tsang can be reached on 571-272-0562 and Janet Andres can be

reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 4131